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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,068	11/14/2003	Meng Yang	312762002710	2630

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MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/714,068	YANG ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 37, 39 and 40 are pending in the application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/25/07 has been entered.

Response to Amendment

The rejection of claim 37 under 35 U.S.C.102 (b) is maintained for reason set forth of the record mailed on and further discussed below.

The rejection of claims 39 and 40 under 35 U.S.C.112 1st paragraph has been withdrawn in view of the new ground of rejection under 35 U.S.C.103 (a) for reasons discussed below.

Response to Arguments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Contag et al.

In response to this rejection, Applicants argue that in column 12 line 19 of Contag does not describe any method for screen for a modulator of the expression of a gene in a multi-cellular

organism by comparing expression of a fluorophore under the directed of the promoter of an endogenous gene in the presence or absence of a modulator. Applicants assert that Contag teaches a gene encoding a light generating molecule under the control of a selected promoter which is effective in cells to be targeted by a therapeutic gene is monitored. Applicants assume that the promoter is on the same vector as a therapeutic gene, and questions how the production of light generating molecule is able to determine not only the location of the therapeutic gene but also the level of expression of the therapeutic gene. Applicants assert that the therapeutic gene is not under the control of the same promoter, and question how this is achieved. Applicants further assert that the paragraph in column 14, beginning at line 58, is more related in that an endogenous promoter is indeed used to drive the production of luciferase, wherein the claim excludes luciferase as an autofluorescent. Applicants further assert that the teaching in column 9, beginning line 29, does not teach how the alternative fluorescent molecules are to be used, because some molecules, such as fluorescein, cannot be generated by the action of a promoter. Applicants further assert that the coupling of an endogenous promoter to a fluorescent protein in Contag is not inevitable result, whereas only the coupling of the luciferase to an endogenous promoter is inevitable result.

The above arguments have been fully considered but deemed unpersuasive. The detailed teaching of Contag et al. and the reason for the rejection were discussed in detail in the previous office actions. In response to the argument raised above, Applicants are reminded that one can not pick and choose portions of the text from the reference that do not meet the claim limitation. Rather, the teaching of the entire document should be considered. Claim 37 comprises three method steps: a) administering a test substance to a non-human multi-cellular organism which

expresses a fluorophore under the direction of a promoter of an endogenous gene, and determine the expression of the promoter by observing the presence, absence or intensity of the fluorescence generated by said fluorophore by whole body external fluorescent optical imaging, b) determine the expression of said promoter in a control animal, c) comparing the expression in a) and b). Contag et al. teach, for example, in col.4 2nd paragraph, a noninvasive method for detecting the localization of a promoter induction event in an animal made transgenic or chimeric for a construct including a gene encoding a light generating protein under the control of an inducible promoter. Contag et al. state that the promoter induction event includes the administration of a substance which directly activates the promoter, the administration of a substance which stimulates production of an endogenous promoter activator, and the animal is imaged. The teaching from col.9, lines 29-32, further defines light generating protein, which clearly includes GFP. The question of how to use some molecules such as fluorescein is irrelevant to the instant rejection because the instant issue is fluorescent protein, and one can appreciate that GFP may be linked to a promoter to be used in the method as described in col.4. As such, the teaching of Contag anticipates the claimed invention. The examiner does not quite understand the question of the therapeutic gene which requires the determination of location and the level of expression of the therapeutic gene. The claims recite disease or treatment have been canceled by the instant amendment, whereas claim 37 does not have the limitation of determine the location and the expression at the same time in an animal. As such, whether this teaching is disclosed in Contag is not relevant to the instant claim. For reasons discussed in the previous office action and above. This rejection is maintained.

New Ground of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Contag et al., in view of Lin et al (US 6380458).

Contag et al. teach, for example, in col.4 2nd paragraph, a noninvasive method for detecting the localization of a promoter induction event in an animal made transgenic or chimeric for a construct including a gene encoding a light generating protein under the control of an inducible promoter. Contag et al. state that the promoter induction event includes the administration of a substance which directly activates the promoter, the administration of a substance which stimulates production of an endogenous promoter activator, and the animal is imaged. The teaching from col.9, lines 29-32, further defines light generating protein, which includes GFP.

However, Contag et al. do not teach the compound administered is a mutation inducing agent or treatment which can cause a mutation in germ-line cells of the multi-cellular organism so that the mutation is stably transferable to offspring of the multi-cellular organism.

Lin et al. teach method of identify compounds that affect expression of the genes by using transgenic zebra fish comprising a promoter from an endogenous gene, for example, GATA1, linked to GFP (see col.11, lines 62-64, and last paragraph of col.10 to 1st paragraph of col.11). Lin et al. teach that the test compounds can be administered to the transgenic fish to

assess the compound on the expression of gene of interest, and comparing the expression to a control zebra fish such that the effect of the compound can be determined (see bridging col. of 10-11). Lin et al. further teach method of identifying genes that affect the expression of fish genes by using transgenic fish carrying the construct of comprising a promoter of a fish gene and a reporter gene, comprising introducing the mutation into the transgenic fish and comparing the expression of the reporter gene to a fish without the mutation (see col. 11, lines 10-18). Moreover, Lin et al. teach that chemical mutagenesis in zebra fish genome generated more than one thousand different mutants with defects in developmental processes (See col. 11, lines 16-29).

Both Contag and Lin et al. teach using multi-cellular organism comprising a construct that comprises a promoter from an endogenous gene operably linked to a reporter protein, such as GFP for identifying expression modulators or test compounds that affect the expression of the endogenous gene. This teaching reflects that it is well known at the time of filing to use transgenic or chimeric multi-cellular organism ranging from zebra fish to mouse that comprises a construct containing a promoter from an endogenous gene linked to a reporter to identify test compounds that affect the expression of the endogenous gene. Both Contag and Lin et al. teach the use of GFP as reporter, indicating it is a commonly used reporter. Contag et al. further teach that the fluorescent generated from GFP may be detected by external imaging. While Contag et al. does not teach administering a mutation inducing agent that affect the expression of a endogenous promoter, Lin et al. suggested that the transgenic fish carrying the reporter may be used to detect mutation that affect the expression of the promoter, and further taught chemical mutagenesis that results in mutation of the gene. By looking at the teaching as a whole, it would

have been obvious to one of ordinary skill of art to use mutation inducing agent or treatment to induce mutation in a multi-cellular organism that carries the construct with a reporter gene and a promoter of interest, and determine whether the mutation affect the promoter expression by measuring the reporter gene expression. One of ordinary skill in the art would use external imaging to detect the fluorescent to detect such expression since it is taught by Contag et al. and such procedure would be non-invasive. Applying known techniques to a system to yield predictable results is obvious to one of ordinary skill of art. Therefore, the claimed invention would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER